

WHAT IS CLAIMED IS:

1. A method of stimulating bone formation in an individual, comprising the step of:

5 inducing an interaction between Smad1 and a homeobox-containing transcription factor, wherein said interaction induces a BMP-responsive gene encoding a bone matrix protein which produces osteoblast and/or chondroblast differentiation thereby stimulating bone formation.

10 2. The method of claim 1, wherein said interaction is induced by means selected from the group consisting of phosphorylation of Smad1, overexpression of Smad1, and mutation of said homeobox-containing transcription factor.

15 3. The method of claim 1, wherein said homeobox-containing transcription factor is selected from the group consisting of Hoxc-8, Hoxa-9, Msx-1 and Msx-2.

4. The method of claim 1, wherein said BMP-responsive gene is selected from the group consisting of osteopontin, sialoprotein, osteonectin, and osteocalcin.

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5. The method of claim 1, wherein said individual is osteopenic.

6. A method of inducing gene(s) encoding bone matrix proteins, comprising the step of:

inducing an interaction between Smad1 and a homeobox-containing transcription factor, wherein said interaction results in an induction of gene(s) encoding bone matrix proteins.

7. A method of inducing a gene encoding osteopontin, comprising the steps of:

inducing an interaction between Smad1 and Hoxc-8, wherein said interaction results in removing transcriptional repression of a gene encoding osteopontin, thereby inducing said gene encoding osteopontin.

8. The method of claim 10, wherein said interaction is induced by means selected from the group consisting of phosphorylation of Smad1, overexpression of Smad1, and mutation of
5 said homeobox-containing transcription factor.

9. A method of screening for a compound that stimulates bone formation, comprising the steps of:

10 contacting a cell with a compound; and
determining the ability of said compound to inhibit binding of Hoxc-8 to a gene, wherein inhibition of binding results in induction of said gene, thus indicating that the compound stimulates bone formation.

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10. The method of claim 9, wherein said compound is selected from the group consisting of an antibody or fragment thereof, synthetic drugs, synthetic proteins and a phosphorylated
20 form of Smad1 or fragments thereof.

11. The method of claim 9, wherein determination of inhibition of binding of Hoxc-8 to a gene is by a method selected from the group consisting of a gel-shift assay, transcription, Northern blotting, and Western blotting.

12. The method of claim 9, wherein said gene is selected from the group consisting of osteopontin, sialoprotein, osteonectin, and osteocalcin.

13. A method of regulating disease in an individual, comprising the step of:-
inhibiting the binding of a homeobox-containing transcription factor to a gene involved in regulating disease in cells of said individual, wherein inhibition of binding removes transcriptional repression by the homeobox-containing protein of said gene, thereby resulting in the induction of said genes involved in regulating disease.

14. The method of claim 13, wherein said inhibition is due to the presence of a compound that binds to the homeobox-containing transcription factor, thereby inhibiting the DNA binding ability of said homeobox-containing transcription factor.

15. The method of claim 13, wherein said compound is selected from the group consisting of an antibody or fragment thereof, synthetic drugs, synthetic proteins and a phosphorylated form of Smad1 or fragments thereof.

16. The method of claim 13, wherein said homeobox-containing transcription factor is selected from the group consisting of Hoxc-8, Hoxa-9, Msx1, and Msx2.

17. The method of claim 13, wherein said individual has a disease selected from the group consisting of osteoporosis, cancer, cardiovascular disease and neurological disease.